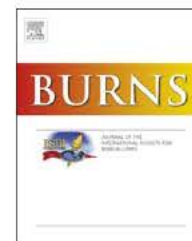


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Central nervous system infections in patients with severe burns[☆]

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ABSTRACT

Background: Central nervous system (CNS) infections develop in 3–9% of neurosurgical ICU patients and 0.4–2% of all patients hospitalized with head trauma. CNS infection incidence in burn patients is unknown and this study sets out to identify the incidence and risk factors associated with CNS infections.

Methods: A retrospective electronic chart review was performed from 1 July 2003 to 30 June 2008 evaluating inpatient medical records along with cerebrospinal fluid (CSF) microbiological results for the presence of CNS infection. The presence of facial and head injuries and burns, along with intracranial interventions were reviewed for association with CNS infections.

Results: There were 1964 admissions with 2 patients (0.1%) found to have CNS infection; 1 each with MRSA and *Acinetobacter baumannii*. Both patients had facial burns and trauma to their head that required intracranial surgery. Of note, both patients had bacteremia with the same microorganisms isolated from their CSF and both survived. Of all patients, 29% had head or neck trauma and burns; 0.35% of those had a CNS infection. Scalp harvest for grafts or debridement of burned scalp was performed on 125 patients of which 9 had an invasive surgical procedure that involved penetration of the skull. The 2 infected patients were from these 9 intracranial surgical patients revealing a 22% infection rate.

Conclusion: The incidence of CNS infections in patients with severe burns is extremely low at 0.1%. This rate was low even with head and face burns with trauma unless the patient underwent an intracranial procedure.

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1. Introduction

Infections are a leading cause of morbidity and mortality among patients who suffer severe burns [1–3]. Classic sites

affected by infection in the setting of burns are skin, respiratory tract (including sinuses), eyes, urinary tract, veins (septic thrombophlebitis), heart (infective endocarditis), peritoneal cavity, and rarely the central nervous system

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(CNS) [2]. CNS infections in patients without burns, such as bacterial meningitis, are typically community onset with infections due to *Streptococcus pneumoniae* and *Neisseria meningitis*. In the case of head trauma resulting in shunts or direct CNS penetration, nosocomial infections can occur with gram negative organisms (over 50% of cases) such as *Pseudomonas aeruginosa* and *Acinetobacter*, and also *Staphylococcus* species (25% of cases) [4–6]. The rate of developing nosocomial meningitis is rare in the hospital without antecedent head trauma or prior infection [7,8]. Burn reviews have reported facial burns and head trauma as being associated with CNS infection [4]. There are several case reports that correlate burns with brain abscesses [9]; however, incidence and etiologies are not known. A post mortem study examining CNS complications of thermal burns from 1992 reported 10.1% of cases with brain abscess; however, this finding was not present in a more recent burn autopsy review [2]. Current published literature is not available and prior literature fails to identify incidence and rate of CNS infection in association with thermal burns and head injury. We set out to find the incidence of CNS infections in a burn unit and identify any associated risk factors, including facial burns or CNS trauma.

2. Methods

The US Army Institute of Surgical Research Burn Center is a 40 bed burn unit which serves both Department of Defense beneficiaries, including casualties from the wars in Iraq and Afghanistan, and a local civilian population from southern Texas. Burn patient care consists of aggressive resuscitation upon arrival with early wound debridement and skin grafting. Intravenous perioperative antibiotics are administered to patients undergoing surgical procedures, and typically consist of vancomycin and amikacin. Topical antimicrobial therapies are applied to the burns, the selection of which is at the discretion of the attending physician. All patients have central venous access with routine replacement of central lines, typically every 3 days. Patients are cared for in individual rooms under contact precautions during their entire hospitalization.

During the period of 1 July 2003 to 30 June 2008, inpatient electronic medical records were screened for the presence of CNS infection in burn patients and the clinical microbiology records were screened for anyone with a culture obtained from the CNS or from cerebrospinal fluid (CSF). Medical records were reviewed for patient demographics (age, gender, mechanism of injury, site of injury, injury as a result of military operations), percentage of total body surface area burn as well as full thickness burns and body region of burn. Evidence of polytrauma was identified in individual burn patients and all patients with facial or head injuries were identified. Patients with neurosurgical procedures or any surgical procedure involving penetration of the skull, were identified. CSF gram stains, cultures and antibiotic therapy (both systemic and intrathecal), as well as duration of antibiotic therapy were reviewed. CNS infection was defined as one or more positive CSF or tissue cultures, with isolation of specific microorganisms.

3. Results

The total number of admissions to the Burn Unit for thermal burns was 1964 with 694 patients from Operation Enduring Freedom/Operation Iraqi Freedom, 97.8% males and a median age of 38 (range 19–52). Of the 1270 civilian and military (not Operation Iraqi Freedom/Operation Enduring Freedom) patients, 78.8% were males with an overall median age of 54 (range 11–96). From all admissions, 12 patients had suspected CNS infections by chart review, of whom 2 patients (0.1% of all burn admissions) were noted to have bacteria isolated from their CSF culture, confirming CNS infection (Table 1). Both of these patients were Operation Iraqi Freedom/Operation Enduring Freedom soldiers who had sustained facial burns and head trauma requiring intracranial surgery with craniectomies. In addition, both patients had bacteremia with identical microorganisms as isolated from CSF (*Acinetobacter baumannii* and methicillin resistant *Staphylococcus aureus* (MRSA)).

Of all patients with burns who were admitted, 560 (28.5%) had head or neck trauma and burns. Twenty seven patients (4.8% of all those with head or neck burns) also had head or neck trauma. Of 1964 patients admitted, only 0.1% had a CNS infection, 100% of whom also had trauma and burns to the head and neck and were soldiers. One hundred and twenty five patients had a surgical procedure to either harvest the scalp or debride the scalp in the setting of scalp burns, out of which 9 patients had an invasive surgical procedure that involved penetration of the skull. Four out of those 9 patients, received craniectomies and 5 patients had trephination of the skull during the process of debridement. Out of 125 patients with surgical procedures of the head, only two patients, who underwent craniotomies, had evidence of CNS infections. Therefore, scalp harvesting donor sites did not pose an increased risk for development of CNS infections.

4. Discussion

Infections are the leading cause of mortality in patients who sustain severe burns [1–3]. Multiple factors are associated with propensity of infection in burned patient. Extensive destruction of protective cutaneous barrier, presence of necrotic and edematous tissues which tend to harbor microorganism growth, use of equipment for invasive monitoring during resuscitation, and impaired immunity are just a few contributing factors to infection [10]. This study was designed to describe the incidence of CNS infections in the setting of burns and associated risk factors as current data is lacking in the literature. Our study reveals a very low rate of 0.1% for all burn patients, and low rates even in potentially higher risk patient populations, including those with facial/head burns (0.35%) or direct head trauma (1.3%), but high rate (22.2%) if the cranium was penetrated.

Bacterial CNS infections (meningitis) are associated with significant mortality and morbidity, with the majority of acute meningitis cases in the community due to *S. pneumoniae* and *Neisseria meningitidis*, with an incidence of 2–3/100,000 [2,11]. Of all meningitis, the incidence of nosocomial meningitis is reported to be approximately 60% [12]. Approximately 30% of

Table 1 – Characteristics of burned patients with central nervous system infections.

Case	Age	Sex	TBSA burn	Date of burn	ISS	Facial burns	Inhalation injury	Head trauma	Craniotomy	CSF culture organism	CSF protein	CSF glucose	CSF gram stain	Blood isolate	Systemic antibiotics	Intrathecal antibiotics	Outcome
1	20	Male	23%	31 May	24	Yes	Yes	Yes	Yes	9 June- Acinetobacter 12 June- Acinetobacter 13 June- Acinetobacter 14 June- Acinetobacter	98	31	No bacteria	Acinetobacter	Tobramycin	Tobramycin	Alive
											109	<20	No bacteria		Colistimethate		
											147	<20	No bacteria				
											114	<20	No bacteria				
2	21	Male	60%	12 March	50	Yes	Yes	Yes	Yes	10 August- MRSA 11 August- MRSA	147		Gram + bacteria	MRSA	Vancomycin	None	Alive
											126	52	Gram + bacteria				
TBSA total body surface area; CSF cerebrospinal fluid; MRSA methicillin-resistant <i>Staphylococcus aureus</i> ; ISS injury severity score																	

all nosocomial cases are associated with gram negative bacilli, but the most common pathogen involved with bacterial meningitis is *S. pneumoniae* [7,12]. Neurosurgical patients are at an increased risk for development of central nervous system infection due to the severity of their illness, common use of invasive devices and traumatic injuries that are often present [13]. Retrospective reviews of neurosurgical ICU patients revealed an approximate 3–10% incidence of CNS infection mostly with gram negative pathogens such as *Pseudomonas* and *Acinetobacter* species, and MRSA [13–15]. It is known that prior colonization with these organism as well as hospitalization in the ICU setting and use of broad spectrum antibiotics are risk factors for CNS infections [16]. Notably there has been a rise in the report of multidrug resistant gram negative bacterial CNS infections including *Acinetobacter* [1,2,7]. Only one publication, in 1992, focused on incidence of CNS infections in association with thermal burns and causative organisms [4]. This was a retrospective, clinicopathologic study of 139 burn patients who died. Fifty three percent of those patients had CNS complications, of which 16% had CNS infections. *Candida* species, *S. aureus* and *P. aeruginosa* were the causative agents in 80% of the CNS infections in this study. This study demonstrated that risks for development of CNS infections in burn patients were extensive burns, with surface area of body involved in burns >30%, systemic infections, burn wound infections, and *S. aureus* endocarditis. Other reports include individual cases such as brain abscesses association with head burns, believed to result from direct invasion of organisms after deep burns of the scalp [9]. In the burn patient CNS autopsy series above, three microorganisms associated with CNS infection were *Candida* species, *P. aeruginosa* and *S. aureus* [4]. It has been previously documented that most CNS infections result from a systemic source [4], as it was extrapolated from this review with all patients suffering CNS infections found to have bacteremia with the same organism. However, it must be emphasized that a large number of patients in the burn unit suffered from bacteremia in the absence of any CNS involvement. *P. aeruginosa*, *A. baumannii* and *S. aureus* are known nosocomial pathogens in our institution [1,17]. As previously described, meningitis did not correlate with head and facial burns [4]. Most patients with burns who had CNS complications suffered from cerebrovascular lesions, metabolic encephalopathies and a small number of infections [4]. However, acute bacterial meningitis has been reported in the setting of open head trauma and cranial procedures. The organisms commonly associated with post surgical CNS infections are often staphylococci and aerobic gram negative rods [18]. In our study period, 9 patients (0.46% of all patients) underwent a surgical procedure with penetration of the skull; of which 2 patients developed CNS infection (22% of patients with cranial surgical procedures), which correlates with the findings in the literature regarding increased risk for CNS infections in neurosurgical patients.

High number of patients with head and neck burns (28.5% of all burn patients) were identified, 1.3% of all burn patients suffered head trauma. Despite the large number of patients with head/neck burns and injuries, there are a surprisingly small number of patients with CNS infections (0.1% of all patients and 0.35% of patients with head/neck burns). All burn

patients with CNS infections were Operation Iraqi Freedom/Operation Enduring freedom soldiers who sustained head trauma and underwent invasive intracranial procedures that involved penetration of the skull, CNS infections were not identified in the civilian population that was included in the study.

In the absence of systematically collected CSF on patients with systemic infections, it is not possible to correlate whether systemic ongoing infections are associated with concomitant CNS infections or whether these infections were cleared with antibiotic therapy.

In conclusion, CNS infections in burn patients are very rare and comprise of only 0.1% patients with burns and 0.35% of patients with head/neck burns. However, in the small numbers in whom the skull was penetrated during a surgical procedure 22% of the patients became infected. Understanding the incidence of CNS infections in burn patients provides guidelines for preventative, diagnostic and therapeutic actions and address strategies to improve overall burn care.

Conflict of interest

The authors have no conflict of interest to report.

REFERENCES

- [1] Ressler R, Murray C, Griffith M, Rasnake MS, Hospenthal DR, Wolf SE. Outcomes of bacteremia in burn patients involved in combat operations overseas. *J Am Coll Surg* 2008;206:439–44.
- [2] Gomez R, Murray C, Hospenthal D, Cancio C, Renz E, Holcomb J, et al. Causes of mortality by autopsy findings of combat casualties and civilian patients admitted to a burn unit. *J Am Coll Surg* 2009;208:348–54.
- [3] D'Avignon L, Saffle J, Chung K, Canacio L. Prevention and management of infections associated with burns in the combat casualty. *J Trauma* 2008;64:277–86.
- [4] Winkelman M, Galloway P. Central nervous system complications of thermal burns: a postmortem study of 139 patients. *Med (Baltimore)* 1992;71:271–83.
- [5] Tang L, Chen S, Hsu W, Lyu R. Acute bacterial meningitis in adults: a hospital based epidemiological study. *Q J Med* 1999;92:719–25.
- [6] Ramos L, Castedo J, Galvan R, García C, Iribarren J, Jiménez J. Incidence of nosocomial infection in patients with nontraumatic or traumatic coma. *Crit Care* 2008;12:12.
- [7] Weisfelt M, van de Beek D, Spanjaard L, de Gans J. Nosocomial bacterial meningitis in adults: a prospective series of 50 cases. *J Hospit Infect* 2007;66:71–8.
- [8] Lefering R, Paffrath T, Linker R, Bouillon G, Neugebauer E. Head injury and outcome – what influence do concomitant injuries have? *J Trauma* 2008;65:1036–44.
- [9] Suzuki T, Ueki I, Isago T, Nozaki M, Hirayama T, Kawanami O. Multiple brain abscesses complicating treatment of a severe burn injury: an unusual case report. *J Burn Care Rehab* 1992;13:446–50.
- [10] Ansermino M, Hemsley C. ABC of burns: intensive care management and control of infection. *BMJ* 2004;329:221–3.
- [11] Hussein AS, Shafran SD. Acute bacterial meningitis in adults: a 12 year review. *Med (Baltimore)* 2000;79:360–8.
- [12] Khwannimit B, Chayakul P, Geater A. Acute bacterial meningitis in adults: a 20 year review. *SE Asian J Trop Med* 2004;35:886–92.
- [13] O'Shea M, Crandon I, Harding H, Donaldson G, Bruce C, Eikhmetalar K. Infections in neurosurgical patients admitted to the intensive care unit at the University Hospital of the West Indies. *W Ind Med J* 2004;53:159–63.
- [14] Pednonomos M, Tsirantonaki M, Psoma G, Katsarelis N, Koukoulitsios G, Lafazanos S. Early and late onset nosocomial infections in ICU patients with head injury. *Crit Care* 2006;10:99.
- [15] Vartzeli P, Yiambides A, Daskalakis K, Moukas M, Schulpis K, Mandragos K. Comparative study on infection of the central nervous system in patients with head trauma and spontaneous cerebral hemorrhage. *Crit Care* 2008;12:13.
- [16] Ng J, Gosbell IB, Kelly JA, Boyle MJ, Ferguson JK. Cure of multiresistant *Acinetobacter baumannii* central nervous system infections with intraventricular or intrathecal colistin: case series and literature review. *J Antimicrob Chemother* 2006;58:1078–81.
- [17] Albrecht MC, Griffith ME, Murray CK, Chung KK, Horvath EE, Ward JA, et al. Impact of *Acinetobacter* infection on the mortality of burn patients. *J Am Coll Surg* 2006;203:546–50.
- [18] Bleck TP. Nosocomial, Meningitis. *Clin Infect Dis* 2007;9:1–2.